

ATTORNEY DOCKET NO.: 0492611-0315 (MIT 6196)**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Griffith-Cima, et al. Examiner: D. Naff
Serial No.: 09/008,945 Art Unit: 1651
Filed: January 20, 1998
For: TISSUE FORMATION BY INJECTING A CELL-POLYMERIC SOLUTION
THAT GELS IN VIVO

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

DECLARATION UNDER 37 C.F.R. 1.132

We, Anthony Atala, Linda G. Griffith, Charles A. Vacanti, and Keith T. Paige declare as follows:

1. We are the inventors of the subject matter disclosed and claimed in United States patent application Serial No.09/008,945 ('945 application) filed January 20, 1998 and entitled "TISSUE FORMATION BY INJECTING A CELL-POLYMERIC SOLUTION THAT GELS IN VIVO". This application claims priority to United States patent application Serial No. 08/056,140 now issued U.S. Patent No. 5,709,854, by Griffith-Cima et al. entitled "Tissue Formation by Injecting a Cell-Polymeric Solution that Gels In Vivo", filed on April 30, 1993.
2. This Declaration is presented for the purpose of removing from consideration by the Examiner an abstract by Atala et al., entitled "Cartilage Cells as a Potential Treatment for Reflux", American Academy of Pediatrics, 1992 Annual Meeting, Section on Urology Program for Scientific Sessions, San Francisco, CA, Saturday, October 10-12, (1992) (Reference "R"). The conference began on October 10, 1992, at which time the above-referenced abstract was available to the public in this country. The present Declaration is presented in accordance with

Ex Parte Magner, 133 USPQ 404 (CCPA 1961) and *In re Katz*, 215 USPQ 14, 18 (CCPA 1982) and establishes that the allegedly anticipatory material in Reference R was not invented by another.

3. Charles Vacanti and Anthony Atala are two of the inventors on the instant application and are also two of the co-authors of Reference R.

4. Alan B. Retik is the third co-author of Reference R. Dr. Retik is not an inventor of the claimed invention.

5. Linda G. Griffith, Charles A. Vacanti, Keith T. Paige, and Anthony Atala mutually conceived and reduced to practice the invention recited in the claims of the '945 application. Dr. Griffith has changed her name from Griffith-Cima since the parent application was filed.

6. To the extent that Reference R discloses the claimed invention, the authors of Reference R derived this subject matter from us, the inventors of the '945 application. Dr. Retik's co-authors on Reference R communicated the subject matter of the claimed invention to Dr. Retik in connection with preparing Reference R. The authors of Reference R are not the inventors of the subject matter of the '945 application.

7. All statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patents issued thereon.

Anthony Atala
Anthony Atala, M.D.

12-7-01
Date

Linda G. Griffith, Ph.D.

Date

Charles A. Vacanti, M.D.

Date

Keith T. Paige, M.D.

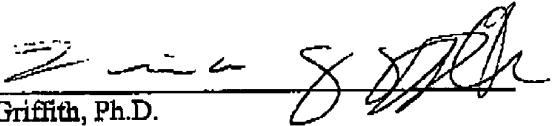
Date

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Anthony Atala, M.D.

Date

Linda G. Griffith, Ph.D.


12/5/01

Date

Charles A. Vacanti, M.D.

Date

Keith T. Paige, M.D.

Date

3339163_1.DOC

Anthony Atala, M.D.

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Anthony Atala, M.D.

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In re Stompel, 113 USPQ 77(CCPA 1957) and establishes conception and reduction to practice of the invention in this country before October 10, 1992.

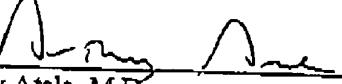
3. The inventors of the claimed subject matter of United States Patent Application Serial No. 09/008,945 are Linda G. Griffith, Anthony Atala, Charles A. Vacanti, and Keith T. Paige. Dr. Griffith has changed her name from Griffith-Cima since the parent application was filed.

4. On a date before October 10, 1992, we conceived and reduced to practice our invention of a cell-polymeric composition for introducing cells into an animal.

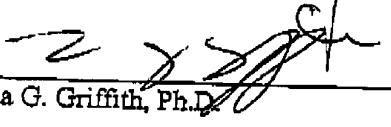
5. Exhibit 1 is a copy of two pages from the laboratory notebook of Anthony Atala, with dates blacked out. Exhibit 1 provides evidence of conception and actual reduction to practice prior to October 10, 1992 of the claimed invention. In particular, page 1 bears notations describing how to combine chondrocytes with alginate. Page 2 describes how the chondrocyte/alginate suspension was injected to specific sites in a mouse to form cartilage tissue. The notes were prepared in the United States of America. The originals of these two pages bear dates prior to October 10, 1992.

7. Exhibit 2 is a typed transcript of the handwritten notes in Exhibit 1. Exhibit 2 is a complete and true transcript of the text of Exhibit 1.

8. All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or any patents issued thereon.


Anthony Atala, M.D.

1/29/02
Date


Linda G. Griffith, Ph.D.

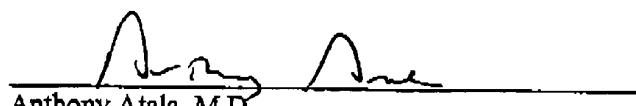
1/5/02
Date

Charles A. Vacanti, M.D.

Date

Keith T. Paige, M.D.

Date
Exchange 3013034.1


Anthony Atala, M.D.

1-29-02
Date

Linda G. Griffith, Ph.D.

Date

Charles A. Vacanti, M.D.

Date

Keith T. Paige, M.D.

Date
Exchange.3013034.]

Anthony Atala, M.D.

Date

Linda G. Griffith, Ph.D.

Date

Charles A. Vacanti, M.D.

CV *1/29/02*

Date

Keith T. Paige, M.D.

Date

Exchanga.3013034.1

Anthony Atala, M.D.

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Linda G. Griffith, Ph.D.

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Charles A. Vacanti, M.D.

Date

Keith T. Paige, M.D.

12/6/01

Date

Exchange 3013034.1

JAN. 29. 2002

5:01PM

CHOATE HALL & STEWART 248-4000

476 4711 W. Kim

NO. 724

P.26

Chordogrs - Bovine

Cell Count \rightarrow 5. \rightarrow 10,000,000 μ cc \rightarrow Media

When my son signs file Tumor with this / one plus
or 4. Adjunct in it. \rightarrow no needle on it
on other occasions \rightarrow 1cc & cell 1cc.
Now a needle for cell 1cc must to tumor
size - 1 cubic cm. \rightarrow per another 19, needle
or 1 cubic cm with 1 repeat. Drawings.

2/10/02 9 a.m. \rightarrow ~~gross~~ frosted \rightarrow 1/4
per. \rightarrow 2/10/02 9 a.m.

White volume reported as 1cc.

Is a 1/2/50 mixture.

~~Hand~~ rings. 5,000,000 μ cc \rightarrow 10,000,000 μ cc \rightarrow 20,000,000 μ cc

1/2 cc



1/2 cc

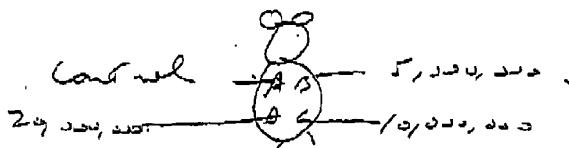
1/2 cc

Exhibit 1

→ placed 0.1cc of Agarose (stabilized) in a Falcon tube -
then pushed it loosely in with about 0.2cc of saline.
drew string out to 0.5cc. and kept aside.

→ Control suspension had \approx 5,000,000 cells/cc $\times \frac{20cc}{1cc} = 100,000,000$ ^{cells/cc}
(unagreed = graded 5ccy media = 20,000,000 cells/cc
→ 3cc of 20,000,000/cc)
push 2cc of saline = 40,000,000 cells total - added Agarose
(→ 4cc of 10,000,000 cells/cc)
push 1/2cc of Agarose = 15,000,000 cells total - added 1/2cc.
(→ 3ccy 5,000,000 cells/cc).

→ placed above 3 suspensions in 5cc strings.
(showed how been divided (1cc each in Falcon tube & 0.3cc air)
also 1sup y media only
→ inserted 0.1cc of just the Falcon string - in air
it was / my error & on 18g needle.



Transcript

Page 1

Chondrocytes-Bovine Cell count concentrated to ten million cells per cc of media.

When ready to inject, fill tuberculin syringes / take plunger out with alginate in it, no needle on it.

On another 3 cc syringe, place one cc of cell suspension.

Stick a needle from cell suspension syringe to tuberculin syringe. Immediately place another nineteen gauge needle on tuberculin syringe. Mix and inject quickly.

2/10 of a cc of powder, should be loose, not tight. Fill to 2/10 of a cc.

Whole volume injected was 0.5 cc.

So this is a 50/50 mixture.

Concentrations injected per 0.5 cc were 5 million, 10 million, and 20 million cells.

A diagram of a mouse showing the injection sites of 5, 10, and 20 million cells as well as a control site.

Exhibit 2